ALBERTA HERITAGE FOUNDATION FOR MEDICAL RESEARCH

FALL 2001

research news

Heritage Mental Health Research

Greater public awareness, new drugs and technologies, and a greater focus on early intervention and prevention by Heritage researchers are providing hope for better mental health for all of us.

A matter of the mind

research news

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AHFMR Mission

AHFMR supports a community of researchers who generate knowledge that improves the health and quality of life of Albertans and people throughout the world. AHFMR's long-term commitment is to fund basic, patient and health research based on international standards of excellence and carried out by new and established investigators and researchers in training.

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What I did on my summer vacation

In her own words (with some editing), Meg Grant, a Grade 12 student at Notre Dame High School in Red Deer and a Heritage Youth Researcher Summer (HYRS) Program 2001 participant at the University of Calgary, tells how she learned how to lay bricks among other things...

I could take this page to tell you how smoking is bad for you. I could tell you that maternal smoking during and after pregnancy increases the risk of SIDS almost sevenfold. I could tell you that 36% of all low-birthweight babies born in the United States are that way because their mothers smoked during pregnancy. I could also tell you that a large number of low-birthweight infants go on to die in their late forties and early fifties of heart disease and stroke.

I think, however, that although the research done in my lab is both new and surprising, if the pictures of diseased lungs and ravaged brains on the cigarette boxes don't keep you from smoking, nothing will. Due to this reasoning, I have decided to fill this page not with what my lab has learned during the course of our experiments, but with what I have learned during the course of working in the lab.

I was lucky enough to be given Dr. Shabih Hasan as my mentor. I say lucky, because Shabih alone has changed my view of medicine so drastically that I feel everyone interested in the field should talk to him first. I've wanted to be a surgeon since the eighth grade—and still do—but until I met Dr. Hasan, I was unappreciative of what it takes to be a medical professional or researcher. You see, it works like this: Everyone interested in medicine must have at least two years of an undergraduate degree. Some enter medical school, which takes three to four years to complete, depending on the program, before they can enter their residency. Other people want to pursue medical research as a Ph.D., which also requires at least four years of studies. Those who graduate from medical school are recognized as medical doctors: M.D.s. Most M.D.s become your standard physician, working in a clinic or hospital like the people on the TV show ER. These doctors may work very few to very many hours, but they are well rewarded, in terms of salary, for their hard work. People with Ph.D.s in a biomedical field often decide to become researchers. These researchers work very many hours and are paid less than physicians, unless they discover something amazing, which is very rare. An example of this would be the people racing to sequence the human genome. Although the clinical aspect of medicine is considered somewhat commercial, the research side is very stressful.

There is a third alternative, however, as some M.D.s are also medical researchers. Here is where my respect for Dr. Hasan comes from. Shabih works up on the fifth floor in the paediatric department. After work, he comes down to our lab to make sure everything is all right. When on call, Shabih spends his time helping out in our lab, waiting for his pager to beep him back up to the fifth floor. I have worked twelve-hour days in his lab, and left before Shabih did... even when he knew that he would have to work again the next morning. Now, I'm not suggesting this line of work is for everyone. In fact, there are fewer than one hundred doctors at the Foothills Hospital who do both clinical work and medical research. It is necessary, however, to recognize that while doctors in the hospital are saving lives, doctors in the labs are saving lives as well.

The first thing that struck me after a week in the lab was how different science was than I had originally thought.

The first thing that struck me, after a week in the lab, was how different science was than I had

ABOVE: MEG GRANT, HYRS 2001 PARTICIPANT

Page 2 ▶

originally thought. You see, real-life science isn't anything like it is in high school. You can't just fool around in the lab and then, for your data, make up numbers that loosely resemble the expected results. In medical research there really are no expected results. As a research scientist, there is no typed-out procedure telling you when to add what or how long to do such and such a thing. You come up with your own aims, your own materials, your own procedures. If you don't take into account certain variables or other confounders, your peers will point it out, your data will be useless, and you won't get any more funding. The funding issue is key. Now don't get me wrong, the life of a research scientist isn't all that bad. As long as you're careful, and within certain limits, you get to make your own hours, research what you want to research, and decide how to spend hundreds of thousands to millions of dollars.

I think that the most important thing I will take back with me from the lab is my new appreciation for knowledge. I have worked in excess of two hundred and ten hours in this lab, collecting data, measuring food, and weighing rats. I found effects of maternal smoking that will probably never make it into the newspaper. I collected data that will seldom be viewed, and have written essays that will be infrequently read. I have also, however, helped to set one, single brick in a wall that will never cease to grow. I placed a brick that had to be there before another one could be placed on top. Some may say one brick among millions is nothing, but with the knowledge I've gained in this lab I know that I will add more bricks in the future, and one day stand back and see what a magnificent and limitless wall I've helped to build.

Medical researchers say that because cancer occurs in so many forms, it's unlikely there will ever be one "magic bullet" to cure or treat all cancers. But how about a bullet that targets 85% of cancers?

Aiming

Such a treatment is at least a decade away, but its promise is becoming clearer, thanks to research being done by a member of the University of Calgary's Cancer Biology Research Group, Heritage researcher Dr. Tara Beattie. Recruited to the University of Calgary in November 2000 from the Ontario Cancer Institute, Dr. Beattie credits Dr. Lea Harrington, her post-doctoral supervisor there, and Dr. Rick Collins, her Ph.D. supervisor at the University of Toronto, with sparking her interest in catalytic RNAs and RNA structure.

Enzymes are a large group of molecules, produced by living cells, that act as catalysts in bringing about the diverse chemical reactions upon which life depends. The enzyme that Dr. Beattie is investigating is the little-known but ubiquitous telomerase, without which humans and all living organisms except for bacteria would gradually die out. Telomerase is a type of enzyme, termed a reverse transcriptase, which causes replication of DNA (deoxyribonucleic acid), the process which enables cells to divide and proliferate.

Telomerase is unique in that it directs the DNA synthesis of only the chromosome tips (called telomeres), not the entire chromosome. "The ends of our chromosomes would keep getting shorter and shorter if telomerase didn't come in and maintain them," Dr. Beattie explains. When laboratory mice are genetically modified so that they no longer produce telomerase, they manage to keep reproducing until the sixth generation. Then, however, the

"If you can inhibit telomerase and stop its activity, you might be able to stop the growth of tumours."

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"If you can inhibit telomerase and stop its activity, you might be able to stop the growth of tumours."

ABOVE: DR. TARA BEATTIE

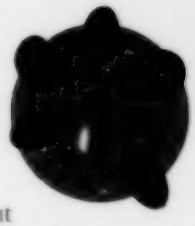
telomeres become critically short and the mice are no longer fertile. It's "game over" in terms of survival.

Very few adult cells contain telomerase activity, since they are not actively dividing, except in the testes—and in rapidly dividing cancer cells.

When cells become cancerous and start forming tumours, they actually "up-regulate": they switch on telomerase activity in order to maintain the chromosomes and keep the cells dividing. "Telomerase is present in the tumour, but is completely inactive in the normal tissue," Dr. Beattie notes. So, "if you can inhibit telomerase and stop its activity, you might be able to stop the growth of tumours."

The medical implications are huge, considering that telomerase is active in at least 85% of cancers, including those of the breast, prostate, and lungs, as well as certain leukemias.

Shutting down telomerase activity by means of a drug which specifically targets the enzyme could be used to enhance other forms of treatment. Granted, a telomerase "switch-off" drug would be ineffective in about 15% of cancers, where tumour cells without telomerase keep dividing by an alternative pathway. "But if you can have some adjunct therapy that hits 85% of tumours, I think that's pretty good statistics," Dr. Beattie says.



Before researchers can figure out how to make telomerase stop working, however, they need a detailed understanding of how the enzyme functions, especially how its RNA and protein components interact. "We don't know what a lot of the peripheral parts of the telomerase molecule look like, or how they're folded, or what they're doing," Dr. Beattie says. "The problem with telomerase is, it is so active and you need so little of it to get activity, you have to really be inhibiting most of it in the cell. Even the smallest amount of activity will still let a cell propagate."

Dr. Beattie's ultimate goal is to develop a reliable in-vitro system to tease apart the enzyme's molecular interactions. "I want to make it and put it back together," she says. "You have to figure out the mechanisms of how it works before you can figure out how to make it stop working." She has spent several years essentially chopping up the telomerase molecule, making different truncated forms of it and determining which parts of its protein are active in assembling the ends of chromosomes. "We think we've identified a part of the protein that's important in recognizing the telomeric DNA," Dr. Beattie says.

This is significant, because it brings researchers one step closer to preventing telomerase from finding and synthesizing the DNA inside a cancer cell. Without this synthesis, the cell can't divide. Hence, the tumour can't grow.

"I never started working on telomerase to cure cancer; however, the fact that there's an implication there just kind of makes what you're doing all the more worthwhile."

Dr. Tara Beattie is an AHFMR Scholar who is an Assistant Professor in the Department of Biochemistry and Molecular Biology at the University of Calgary. *Dr. Beattie has also received support from the National Cancer Institute of Canada.*

Recent publications:

Beattie TL, Zhou W, Robinson MO, Harrington L. Polymerization defects within human telomerase are distinct from telomerase RNA and TEP1 binding. *Molecular Biology of the Cell* 2000; 11:3329-3340.

Beattie TL, Zhou W, Robinson MO, Harrington L. Reconstitution of human telomerase activity in vitro. *Current Biology* 1998; 8:177-180.

Beattie TL, Zhou W, Robinson MO, Harrington L. Functional multimerization of the human telomerase reverse transcriptase. *Molecular and Cellular Biology* 2001. In press.

It *isn't* all in your head

Those are familiar words to anyone who has ever suffered a panic attack.

And they're no consolation at all for the 3% of the population who experience anxiety so crippling that it stops them in their tracks.

Research has now shown that there is a direct link between panic and anxiety disorders and a neurotransmitter known as GABA that is prevalent throughout the brain. "Research in animals shows that early life stress seems to reduce the activity of the GABA system," says AHFMR Clinical Health Investigator and psychiatrist Dr. Nick Coupland, a specialist in anxiety disorder and depression at the University of Alberta. "There are changes in GABA function in the parts of the brain that may regulate stress responses. We're interested to know if this is true in humans as well, and if this plays a part in how early life stress predisposes people to depression and anxiety."

To test this hypothesis, Dr. Coupland has recruited volunteers who suffer from panic disorder, along with a control group of individuals for whom anxiety is not a significant problem. He "challenges" the participants by giving them a medication called flumazenil. "About 50% of the people who tend to have panic attacks will have one in response to the agent, whereas the healthy people don't," says Dr. Coupland. "There are lots of other measures that should change in a certain way if the attack is a chemical effect, so we should be able to see whether it's due to a chemical effect or a psychological mechanism."

Separate research with the University of Alberta's Department of Biomedical Engineering is developing measures of the levels of GABA in the brain using an imaging technique known as NMR spectroscopy, which will then be used to study differences in patients with anxiety and depression.

Female hormones and anxiety

The research interests of Dr. Jean-Michel Le Mellédo, another psychiatrist–researcher at the University of Alberta, focus on anxiety and mood disorders. More specifically, he is interested in three areas that frequently overlap: mood and anxiety, the cardiovascular system, and sex hormones.

The AHFMR Population Health Investigator is an expert on premenstrual dysphoric disorder (PMDD), the significant mood, behavioural, and physical symptoms associated with the menstrual cycle. Not all women suffer from PMDD, but those who do are at high risk of more serious behavioural or psychiatric problems, such as major depression, anxiety disorders, and postpartum depression. Fluctuations of the female hormone progesterone and a related hormone, allopregnenolone, during the menstrual cycle affect the GABA system and may contribute to the symptoms of PMDD.

Dr. Le Mellédo uses flumazenil to challenge the GABA system in women with the disorder during the beginning of the menstrual cycle (when premenstrual symptoms are absent) and during the days before the menses (when premenstrual symptoms are present). His purpose is to determine in women with PMDD if the GABA system is disregulated during the whole menstrual cycle or only when they experience premenstrual symptoms. In collaboration with Dr. Glen Baker, a neurobiochemist at the University of Alberta, he also compares allopregnanolone levels of women who suffer from PMDD with those of unaffected women, to see if the women with PMDD have lower levels of this naturally occurring anti-anxiety agent.

Not all women suffer from PMDD, but those who do are at high risk of more serious behavioural or psychiatric problems.

"PMDD is an ideal way to study the relationship between mood and anxiety and the hormonal changes that are occurring," says Dr. Le Mellédo. "In two weeks, women who suffer from PMDD reach a state of perfect well-being. Then, within two weeks, they are in a state of anxiety and distress. It's important to know exactly why this is happening, so we can develop new treatments for the many women who suffer from the disorder."

DR. JEAN-MICHEL LE MELLÉDO (L) AND DR. NICK COUPLAND (R)

Dr. Nick Coupland is a Heritage Clinical Investigator, Assistant Professor of Psychiatry at the University of Alberta, and Director of the Psychopharmacology Research Unit. His research is also supported by the CIHR, the Canadian Psychiatric Research Foundation, and the University of Alberta Hospital Foundation.

Dr. Jean-Michel Le Mellédo is a Heritage Clinical Investigator, Assistant Professor in Psychiatry at the University of Alberta, and Director of the Mood and Anxiety Research Unit. His research is also supported by the CIHR and the University of Alberta Hospital Foundation.

Most recent publications:

Coupland NJ. Social phobia: etiology, neurobiology and treatment. *Journal of Clinical Psychiatry* 2001; 62(suppl.1):25-35.

Le Mellédo J-M, Bradwejn J, Koszycki D, Bellavance F, Bichet D. Arginine-vasopressin and oxytocin response to cholecystokinin-tetrapeptide. *Peptides* 2001; 22:1349-1357.

ARTWORK FACING PAGE: JANET CARDIFF. *THREE THOUGHTS*. ETCHING ON PAPER. 27.6 X 61.4 CM. 1994. COURTESY OF THE ALBERTA FOUNDATION FOR THE ARTS.

Debunking heart

Dr. William Ghali's work seems to have put him in the business of debunking myths. Using a data collection tool called APPROACH (the Alberta Provincial Project for Outcome Assessment in Coronary Heart Disease), Dr. Ghali is taking a new look at some pre-conceived ideas relating to sociodemographic factors and access to cardiac procedures.

APPROACH is an ongoing data-collection initiative developed by cardiologist Dr. Merrill Knudtson, a recipient of support from the Health Research Fund. Since January 1995, cardiologists, nurses, and technicians across the province have been collecting information on patients who undergo heart catheterization procedures (the passage of a small, flexible instrument through a vein into the heart, in order to secure blood samples and determine cardiac abnormalities) and tracking these patients over time. A member of the new Centre for Health and Policy Studies at the University of Calgary Faculty of Medicine, Dr. Ghali has been using APPROACH to examine such factors as age, gender, ethnicity, socioeconomic status, occupation, location of residence, work status, clinical outcomes, and certain aspects of quality of life in the likelihood of a patient undergoing cardiac care.

"When we account for the clinical differences between men and women there is no bias in the care they are receiving. A very good finding for the sake of equity in our healthcare system."

In a number of prior studies examining gender differences in this context, it had been found that women were less likely to have heart catheterizations, bypass surgery, or angioplasty (the surgical reconstruction of blood vessels). "A number of people have pointed to those findings and said that there may be physician bias or bias against women, and there may not be equitable access to available cardiac services," says Dr. Ghali. "Another interpretation has been that it may be clinical differences between men and women that account for differences in procedure rates, not an actual discrimination against women."

Using APPROACH, Dr. Ghali found that men were 1.5 times as likely as women to undergo revascularization procedures–bypass surgery or balloon angioplasty–after receiving an angiogram (a technique used to show the detail of blood vessels). The initial findings, taken by themselves, would have left the impression of gender bias. Dr. Ghali was able to look deeper however, using the rich clinical data available through the APPROACH database. Once influencing factors such as the extent of blockage in the heart arteries and the presence or absence of diabetes were factored into the results, the differences in treatment disappeared. "When we account for the clinical differences between men and women, there is no bias in the care they are receiving," says Dr. Ghali. "A very good finding for the sake of equity in our healthcare system." He emphasizes, however, that his study examined only the decision-making after catheterization had occurred, and points out that there may still be inequities in pre-catheterization treatment.

Dr. Ghali went on to challenge the hypothesis that people living far away (more than 450 km) from a patient-care centre are less likely to undergo heart procedures. Using postal codes to calculate how far individuals lived from a hospital, he found that the reverse was actually true: people living more than 450 km from a hospital were 5% to 10% more likely to undergo revascularization procedures shortly after diagnostic catheterization than patients living closer to a centre. "What we think our results are telling us is that there is a tendency, when people live far away, to go for a definite or a more reassuring fix of the problem rather than just a wait-and-see kind of approach," summarizes Dr. Ghali. "But when we look again at population rates of catheterization for the people who live far away, they are actually less likely to have a

AP

health myths

catheterization in the first place. They are less likely, perhaps, to get into the system. Once they're in, they go all the way to the definite treatment more quickly."

Dr. Ghali's subsequent study of the age factor was less focused on access and more on outcomes. Because bypass surgery is expensive and drains health system resources, some may question the value of performing this procedure on individuals late in life. As Dr. Ghali points out, thousands of children can be vaccinated for the cost of one bypass procedure. But proponents of performing the procedure on the elderly suggest that comparisons shouldn't be made between older and younger patients, but between older patients who receive the procedure and those who do not. "We find that in absolute terms, the difference in outcome for those who are treated aggressively with revascularization and those who aren't is actually greatest in those in the 80 years and older group," says Dr. Ghali. "How that translates into life-years gained still needs to be studied, but paradoxically, the absolute benefit may actually be the greatest in the older patients." He states that an important observation made through the use of APPROACH is that decisions on providing cardiac care to the elderly should not be based on chronological age but on biological age, in conjunction with a full assessment of the patient's clinical situation.

Dr. Ghali has been using APPROACH to examine factors that might influence the likelihood of a patient undergoing cardiac care.

In another strand of his study, Dr. Ghali examined rates of access to cardiac catheterization in aboriginal reserve populations, using census data. Again, the cursory results showed that aboriginals receive this procedure at only about half the rate of the rest of the population. However, once data was factored in to account for such things as the younger age of populations on reserves, gender differences, and the more rural population living farther from patient-care centres, the procedure rates were almost the same. People living on reserves are, indeed, less likely to undergo heart procedures, but not because of their ethnicity per se, says Dr. Ghali.

Dr. Ghali is currently examining income and employment status as factors in receiving cardiac care. He plans to share all of his information with decision-makers and health policy planners—where it can best be used to make a difference.

Dr. William Ghali is an Associate Professor in the departments of Medicine and Community Health Sciences at the University of Calgary. *He receives support from the Health Research Fund administered by AHFMR on behalf of Alberta Health and Wellness, as well as from the Heart and Stroke Foundation, the Canadian Diabetes Association, and the Canadian Institutes of Health Research.*

Recent Publications:

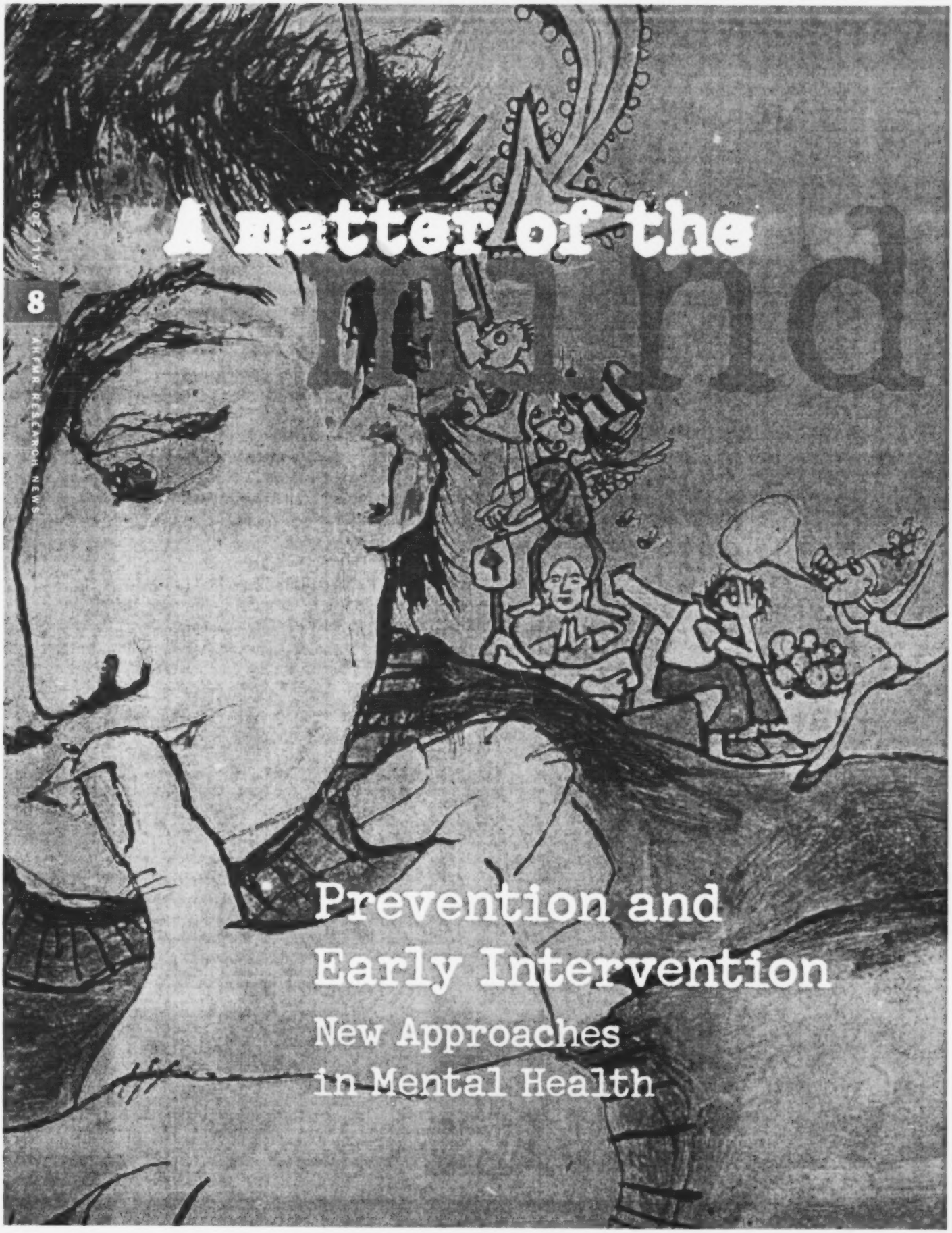
Ghali WA, Faris PD, Galbraith PD, Norris CM, Curtis MJ, Saunders LD, Dzavik V, Mitchell LB, Knudtson ML. The importance of detailed clinical data for evaluating sex differences in access to cardiac revascularization. *Journal of General Internal Medicine* 2001; 16(Suppl 1):134.

Ghali WA, Faris PD, Galbraith PD, Norris CM, Knudtson ML. Aboriginal ethnicity and access to cardiac procedures. *Journal of General Internal Medicine* 2001; 16(Suppl 1):134.

Graham MM, Faris PD, Ghali WA, Knudtson ML, on behalf of the APPROACH Investigators. Long-term outcome of revascularization or medical therapy in a cohort of elderly patients. *Journal of the American College of Cardiology* 2001; 37(Suppl A):194A.

LEFT: DR. WILLIAM GHALI

PROACH



8
AHFMR RESEARCH NEWS
FALL 2001

"There's been a convergence of public attitudes and the technology available to treat mental illness," says AHFMR researcher Dr. Donald Addington, Professor and Head of the Department of Psychiatry at the University of Calgary.

Increased public awareness, as well as more effective medications with fewer side effects, have lifted some of the barriers to treatment and helped to erode the stigma that tended to keep those who suffered from mental illness in the shadows. These changes present AHFMR clinical researchers with an opportunity to make a difference. They can shift their focus to where they believe their efforts will have the most impact—early intervention and, whenever possible, prevention. Their studies provide hope, not only for individuals who suffer from mental illness, but for the mental health of our population as a whole.

Minimizing the impact of schizophrenia

Dr. Donald Addington and Dr. Jean Addington, a psychologist and Associate Professor in the University of Calgary's Department of Psychiatry, are researchers in schizophrenia, the illness that most often strikes young people just as they are hitting their stride. The average age of onset is 23 in young men and slightly older in women. The Addingtons' goal is to reach these young people early and minimize the impact of the disease on their lives. "We want to show that we can make a difference in these early stages," says Dr. Jean Addington, "by treating these people before their illness disrupts their lives."

In addition to operating the Early Psychosis Treatment and Prevention Program, a joint initiative by the Calgary Health Region and the Canadian Mental Health Association of Calgary, the Addingtons developed the PRIME (Prevention through Risk Management and Education) clinic, which is supported exclusively by research funds. PRIME aims to identify young people with pre-psychotic symptoms—the subtle, "something is not quite right" symptoms. Two years ago, they started research with PRIME to see whether early education, psychosocial intervention, or medication could either prevent or delay the onset of a more serious psychotic illness. They now believe they have enough

DR. DONALD AND DR. JEAN ADDINGTON

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Finding Ways to Help the Most Challenging Patients

DR. ANTHONY JOYCE

Since borderline personality disorder (BPD) became part of psychiatry's diagnostic bible in 1985, the term has been fraught with controversy. Rather than regarding BPD as a discrete condition, some clinicians view the disorder as a continuum of pathology that is associated with a number of other psychiatric conditions—such as depression, anxiety, and eating disorders.

Controversial diagnosis or not, there is no denying that patients with the disorder experience extreme emotional pain. The majority of them report a history of sexual abuse. They have significant difficulty managing intense emotional states, engage in tumultuous interpersonal relationships, and suffer severe identity problems. As University of Alberta research psychologist Dr. Anthony Joyce says, "They really don't know who they are."

To compound the problem, these patients have a reputation for being notoriously difficult to treat. They may disregard medical advice and ignore prescriptions for anti-depressants; they can be their most cantankerous and disruptive in group therapy. An admission to hospital does little more than give them a few days' respite—at a high cost to the healthcare system.

Controversial diagnosis or not, there is no denying that patients with the disorder experience extreme emotional pain.

Supported by the AHFMR Health Research Fund, Dr. Joyce is working to increase the effectiveness of treatment interventions offered to these patients. In earlier research, two subgroups of patients with borderline personality disorder were found to present particular challenges. One group included those

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information about their ultra-high-risk (for psychosis) group to justify providing treatment services to them; however, there are no funded services for this group to date.

Although they would like to do more prevention work, it can be quite a challenge to find these young people. "For everybody who ends up having a psychotic episode, there's a pre-psychotic person out there," says Dr. Jean Addington. "If you encourage people to get help before they become psychotic, hopefully the symptoms can be controlled before they become severe and more disrupting and disabling."

With support from the AHFMR Health Research Fund, Dr. Don Addington is developing a set of indicators to evaluate early psychosis programs such as theirs, to identify areas where they can be more effective. Although there are very few established indicators in mental health as yet, work in this area is growing. He and his group will use the indicators first to evaluate their own schizophrenia and early psychosis program, then to compare programs across the country. Dr. Addington has also just received significant funding to develop public education about the early onset of psychosis and its recognition.

The Health Research Fund is also providing support to Dr. Jean Addington for a five-year follow-up study of the patients in the Early Psychosis Program. She hopes the study will demonstrate the long-term effectiveness of the Program.

"In terms of mental health, early prevention is new," she says, "and in terms of schizophrenia and psychosis, it's very new. Some of the fear has been that if you try and identify people early, you stigmatize them. But if, for example, you have a history of heart disease in your family, you would want to have the information you need to do what is best for your future health. The same applies to schizophrenia."

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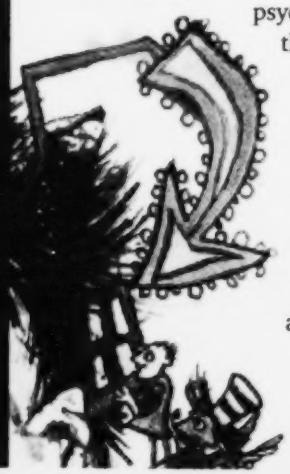

Schizophrenia and brain chemistry

One of the challenges for the Addingtons and others who work in the field of schizophrenia is that individuals can be very ill for a year or even longer—exhibiting the classic symptoms of delusions and hallucinations—and still not be receiving psychiatric help. "That isn't because of waiting lists or anything like that," says AHFMR researcher and University of Alberta psychiatrist Dr. Phil Tibbo. "It's because the individuals aren't recognizing it, family doctors are not recognizing it, and the families themselves aren't recognizing it."

What they are overlooking or unable to recognize are the prodromal symptoms, the precursors of full-blown illness. "We need better ways of being able to identify individuals at risk and predict, by looking at these prodromal symptoms, which of these individuals have schizophrenia," he says. "We know we can do the most for these patients, optimizing their level of functioning, if we get them within the first five years of their illness."

To improve the chances of identifying affected young people before their illness causes them serious problems, Dr. Tibbo is investigating both non-psychotic adolescents and adults at risk for schizophrenia (having a parent or sibling with schizophrenia) compared to normal and psychiatric controls. He is also following the adolescents over time as they enter and pass through the age-of-onset risk period. His research involves brain imaging with magnetic resonance spectroscopy (MRS) as well as a battery of neuro-cognitive and clinical tests. He is particularly interested in the role that neurotransmitters, glutamate and glutamine, play in schizophrenia. Both of these chemicals are present throughout the brain, but they appear in significant concentrations in the medial frontal lobe, and they can be measured with MRS. Research in animals has shown that abnormalities of glutamate may cause cellular damage and changes in behaviour.

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Dr. Tibbo is comparing non-psychotic adolescents and adults "at risk" for schizophrenia (having a parent or sibling with schizophrenia) with normal and psychiatric controls.

ABOVE: DR. PHIL TIBBO

"These kids don't just wake up one day when they're 19 and become schizophrenic," says Dr. Tibbo. "The neurodevelopmental hypothesis about schizophrenia is that there has been something wrong since birth, which causes interactions with normal development of the central nervous system and the brain resulting in the emergence of, psychotic symptoms." This hypothesis is consistent with the findings of animal studies, which have shown that abnormalities of the glutamate and glutamine system, present from birth, produce symptoms that don't appear until the animal reaches adolescence.

Although research has looked at individuals who have had their first episode of schizophrenia or who have chronic problems with the illness, no MRS imaging work has been done with the group Dr. Tibbo is studying. "By working with these people who have not yet experienced a psychotic episode, we can look at what causes the illness, and we can see if there are protective factors," he says. "The goal is to help define better predictors of schizophrenia, so we can start working at better secondary and primary prevention."

Nipping eating disorders in the bud

Years of experience have taught Dianne Drummond that she and her fellow dietitians are often on the front line when it comes to children with eating disorders. "Parents may not be able to convince their kids to see a doctor," says Drummond, the Alberta Mental Health Board's Eating Disorder Promotion and Prevention Specialist for Edmonton and Northern Alberta, "but they may be able to persuade them to get advice on their diet."

Five years ago, Drummond and her co-researcher, Suzanne Hare, received funding from the Grey Nuns' Women's Health Fund to develop a tool that would identify children at risk of eating disorders. "We started the project hoping there would be an available tool that schools could use," says Hare, a clinician dietitian at the Grey Nuns Community Hospital and Health Centre. "We didn't want to look just at eating disorder behaviours. We wanted to look at risk factors." While full-blown eating disorders are infrequent in children, the researchers say, the presence of risk factors is much more common. Dieting, for one, is a huge risk for eating disorders in children.

Drummond and Hare developed and validated the Risk of Eating Disorder Inventory (REDI™), an assessment used by family physicians, psychiatrists, dietitians, and in schools.

Drummond and Hare developed and validated the Risk of Eating Disorder Inventory (REDI™), a tool which is now being used in the offices of a number of family physicians, psychiatrists, and dietitians, as well as in schools. The REDI has also become a springboard for their current project, which will take them into Grade 5 and Grade 7 health classes to prevent eating disorders in schoolchildren. In the two-year project supported by the AHFMR Health Research Fund, Drummond and Hare will develop and pilot a wellness program; revise it according to student feedback;and train educators to deliver it. The program will be based on a parent workbook and a teacher's resource manual they have developed (which is now available on CD).

Because recent literature suggests that going into the schools to talk specifically about eating disorders may trigger copycat behaviours, Drummond and Hare's program focuses on wellness and self-acceptance. "Too often kids think they can make themselves into something that they can't ever be, like someone they've seen on television," says Drummond. "We help them to explore their own genetic body shapes." The researchers also encourage students to cast a more critical eye on the media and evaluate what they are seeing. "Often children (and adults!) think that the picture they see is an accurate likeness," adds Hare. "They don't realize that anything on TV can be digitally altered."

SUZANNE HARE (L) AND DIANNE DRUMMOND (R)

As well as being a welcome resource for schools grappling with the issue of eating disorders, the program will have positive spin-offs for Drummond and Hare. As returning students, they will have a ready-made thesis topic for their upcoming master's degrees.

Preventing relapse of depression...

According to a study conducted by the Harvard School of Public Health and the World Bank, depression is the second leading cause of disease in developed countries like Canada. Dr. Keith Dobson, a professor of Clinical Psychology in the Department of Psychology at the University of Calgary, says his "best estimate" is that at any point in time, 1% of men and 2% of women are suffering from depression.

Dobson admits that his estimate probably errs on the conservative side, and notes that some have pegged the incidence of depression as high as 25%. His figure doesn't include those who experience a mild period of depression, one that is enough to affect their lives but not serious enough to propel them to a therapist's or physician's office. Still, in spite of a greater general awareness of depression and much-lauded improvements in pharmaceutical treatments, he says, "people are not seeking help the way they could be." Even getting help offers no guarantees: approximately 50% of patients treated for depression are likely to suffer a relapse within a year of their recovery.

In a project supported by the AHFMR's Health Research Fund, Dobson and his team of researchers are following a large sample of women who have had clinical depression, assessing them every two weeks for a year after their point of recovery. In those women who suffer a relapse, the researchers look for any medical conditions or changes in thinking that might have been contributing factors.

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Dobson hopes his research will help those who recover from depression only to find themselves clenched in the jaws of the disease again.

ABOVE: DR. KEITH DOBSON

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who had been diagnosed with major depressive disorder but who denied being depressed; and the other consisted of individuals whose difficult interpersonal style made them poor candidates for the group therapy that could help them. At the conclusion of treatment, these patient groups showed less than optimal improvement on measures of depressive symptoms and interpersonal health, respectively.

In the intensive, 18-week group-oriented Evening Treatment Program at the University of Alberta Hospital's Department of Psychiatry, participants undergo a battery of tests to assess all the different elements of depressive illness. "If we can identify different patterns of presentation," Dr. Joyce says, "then we should be able to find some kind of markers for when a prescription of antidepressants would be helpful for those BPD patients who fall in the first group."

The second group, the ones who tend to rub others the wrong way, will receive training to prepare them for the group treatment program. Dr. Joyce hopes that if the patients can be trained to think about their problems differently, rather than fall back on comfortable but harmful patterns of behaviour, it will give them a bit of a jump-start on the group therapy offered in the program.

"The group therapy approach is a good one for these patients. It gives them a place to be held and supported so that the treatment can have an effect. That's important," says Dr. Joyce, "because these people really do suffer."

Dr. Anthony Joyce is an Associate Professor in the Department of Psychiatry at the University of Alberta, and Coordinator of the Research and Evaluation Unit for the Capital Health Authority. *His project on patients with borderline personality disorder is supported by an AHFMR Health Research Grant. He also receives research support from the Canadian Health Services Research Foundation (in conjunction with the AHFMR, the Alberta Mental Health Board, the Institute of Health Economics, and Eli Lilly), the UAH Foundation, the Canadian Institutes of Health Research, and the U.S.-based Group Psychotherapy Foundation.*

Recent publications include:

Piper WE, McCallum M, Joyce AS, Rosie JS, Ogrodniczuk JS. Patient personality and time-limited group psychotherapy for complicated grief. *International Journal of Group Psychotherapy*. In press.

Piper WE, Joyce AS, McCallum M, Azim HFA, Ogrodniczuk JS. Interpretive and supportive psychotherapies: Matching therapy and patient personality. Washington, DC: *American Psychological Association Press*, 2001.

"The prediction of a 50% relapse rate is pretty accurate," says Dobson, who has been studying depression since 1980. In the 135 subjects in his study, the relapse rate has been almost exactly 50%. The challenge is to find a way of predicting who will recover and who will suffer a relapse. Dobson is hoping his research will provide some useful clues as to what can be done for those who seem to recover, only to find themselves clenched in the jaws of depression again.

...and stopping depression before it starts

In other AHFMR-supported research at the University of Calgary, psychiatrist Dr. Scott Patten is using the World Wide Web and interactive voice telephone technology to test interventions aimed at preventing depression, such as cognitive and behavioural techniques, maximizing sleep quality, and reducing drug and alcohol use. Dr. Patten says his intent was to create a cost-effective, confidential way of delivering techniques that reduce the risk of depression. "These are not strategies that would be regarded as treatment strategies, but they are strategies that can help people prevent the intrusion of depression into their lives," he says. "In principle, the program could be accessible to everybody, so that we might have an impact on the level of population health."

When we look to the future of treatment for mental illness, it's important to keep in mind the notions of early intervention and prevention and within the context of population health. "When you look at a problem like depression from a public-health point of view, the priorities are a little bit different than when you are looking at it from a clinical perspective," says Dr. Patten. "Of course, there have been tremendous advances in treating depression. But when you look at that from a public-health perspective, it's immediately apparent that the solution isn't just in developing treatment procedures, because there are a lot of people with depression who will never seek treatment. There is a general principle in public health that prevention, if it can be successfully accomplished, is better than treatment." Early intervention and prevention are not only the way of the future—they're a better way to address the many challenges of mental health. It's as simple as that.

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Dr. Donald Addington's research is supported by the Health Research Fund, administered by AHFMR on behalf of Alberta Health and Wellness. He also receives support from the Calgary Community Lottery Board, the Calgary Health Region/Alberta Mental Health Board and Psychiatric Program, and the Eli Lilly Zyprexa Research Foundation.

Dr. Jean Addington's research is also supported by the Health Research Fund. She also receives support from the Canadian Institutes of Health Research.

Dr. Philip Tibbo is a Heritage Clinical Investigator, Assistant Professor, and Director of the Post-graduate Training Program in Psychiatry at the University of Alberta, as well as Co-Director of the Bebensee Schizophrenia Research Unit. He is also funded by the National Alliance for Research in Schizophrenia and Affective Disorders (NARSAD), the Canadian Institutes of Health Research, and the University of Alberta Hospital Foundation/Alberta Health Sciences Research Institute.

Dianne Drummond and Suzanne Hare's research is supported by the Health Research Fund. They also receive funding support from the Caritas Research Steering Committee, Grey Nuns Community Hospital and Health Centre, and the Capital Health Authority.

Dr. Scott Patten is an AHFMR Population Health Investigator and an Associate Professor in the University of Calgary departments of Community Health Sciences and Psychiatry. He is also supported by the Health Research Fund; the National Health Research and Development Program; and the Canadian Institutes of Health Research.

Dr. Keith Dobson, in the Department of Psychology at the University of Calgary, receives support from the Health Research Fund.

Recent publications by Dr. Donald Addington and Dr. Jean Addington:

Addington J, Addington D. Early intervention for psychosis: the Calgary Early Psychosis Treatment and Prevention Program. *The Bulletin of the Canadian Journal of Psychiatry* 2001; October edition.

Addington J, Jones B, Ko T, Addington D. Family intervention in early psychosis. *Psychiatric Rehabilitation Skills*. (In press.)

By Dr. Philip Tibbo:

Tibbo P, Nopoulos P, Allen P, Valiakalayil A. Home structure of adolescents at high risk for schizophrenia. *Schizophrenia Research* 2000; 41:173.

Tibbo P, Valiakalayil A, Paulson L. Neuropsychological evaluations of high-risk adolescents for schizophrenia. *Biological Psychiatry* 2000; 47(8S):82S.

By Dr. Keith Dobson:

Dobson KS. Chronic processes in depression: differentiating self and other influences in onset, maintenance, and relapse/recurrence. *Clinical Psychology: Science and Practice* 2000; 7:236-239.

Dozois DJA, Dobson KS. Information processing and cognitive organization in unipolar depression: specificity and comorbid issues. *Journal of Abnormal Psychology* 2001; 110:236-246.

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The body's pipelines

The heart and blood vessels carrying oxygen and other nutrients throughout our body get help from a lesser-known—but just as important—network of tiny pipelines. It's called the lymphatic system, an intricate web of pump-equipped vessels and lymphatic glands (called lymph nodes).

The system captures and returns about three to five litres per day of essential body fluids that are circulated into tissues by the cardiovascular system. This lymph fluid, including proteins, infection-fighting cells, and other particles, is pumped back into the bloodstream and carried to the heart to be re-circulated.

"If you didn't have that fluid going back into the bloodstream, your tissues would swell and toxins would build up in your body," says medical researcher Dr. Pierre-Yves von der Weid. Within 30 hours, "you wouldn't have any fluid left in your bloodstream."

When the lymphatic system malfunctions, it causes fluid buildup, swelling tissues and toxin accumulation—a condition called lymphedema. Women with breast cancer whose underarm lymph nodes are removed often experience swollen arms due to lymphedema up to six months after surgery. Although lymphedema usually doesn't become life-threatening, "it's pretty serious and it's not easy to live with," says Dr. von der Weid, Assistant Professor of Physiology and Biophysics at the University of Calgary.

RIGHT: DR. PIERRE YVES VON DER WEID

He is investigating the biological mechanisms, including the intrinsic pumping action, in isolated lymphatic vessels obtained from guinea pig tissue. "I want to understand how the system is working and this model is particularly useful."

Like blood vessels, lymphatic vessels are made from endothelial cells and from smooth muscle cells that provide strength and elasticity. But unlike blood vessels, which flow both ways through the body, lymphatic vessels form a one-way system.

When the lymphatic system malfunctions, it causes swelling tissues, lost fluid circulation and accumulating toxins—a condition called lymphedema.

Each lymphatic vessel comprises numerous individual chambers, isolated from each other by valves. These chambers are able, by first swelling with lymph fluid and then suddenly constricting, to pump the fluid along in the vessel.

"It's like every chamber is like a small heart in its pumping action," Dr. von der Weid notes.

Using a video camera and measuring device, Dr. von der Weid is able to precisely record the change in each vessel chamber's diameter and in the pumping frequency. He can then test drugs, such as norepinephrine or nitric oxide, to see how various substances either slow down or increase the pumping action.

Dr. von der Weid also is investigating the intracellular properties of the lymphatic vessels' smooth-muscle cells. He wants to understand how the cells control the entry of calcium ions from the extracellular space—triggering the vessels' rhythmic contractions. His

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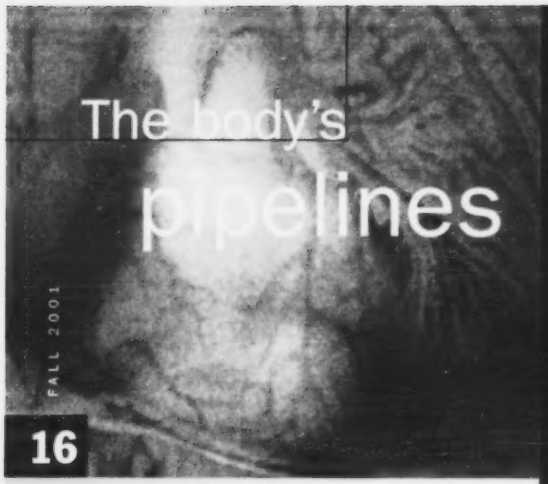

research may lead to drugs that would target the lymphatic vessels. Increasing the vessels' pumping efficiency, for example, could help treat people with lymphedema and other inflammatory disorders.

"Understanding how lymphatic vessels pump is not that simple," Dr. von der Weid says, "but I think we are very close to understanding the basic mechanisms."

Dr. von der Weid is able to precisely record the change in each vessel chamber's diameter and in the pumping frequency.

Dr. von der Weid completed his Ph.D. at the University of Geneva and was recruited to the University of Calgary in November 1999. He says his post-doctoral work with Dr. Dirk Van Helden at the University of Newcastle, in Australia, sparked his interest in the lymphatic system.

Dr. von der Weid is a Heritage Medical Research Scholar who also receives funding from the Heart and Stroke Foundation of Canada.

Recent publications:

von der Weid P-Y. Review article: lymphatic vessel pumping and inflammation–the role of spontaneous constrictions and underlying electrical pacemaker potentials. *Alimentary Pharmacology & Therapeutics* 2001; 15: 1115-1129.

von der Weid P-Y, Zhao J, Van Helden DF. Nitric oxide decreases pacemaker activity in lymphatic vessels of guinea pig mesentry. *American Journal of Physiology–Heart and Circulatory Physiology* 2001; 280: H2707-H2716.

Learning by

Although Abdi Ghaffari has put his university studies on hold, that doesn't mean he's stopped his education. He is "learning by doing", with the help of the Heritage Foundation's Technology Commercialization Internship Program. Ghaffari is working at PulmoNOx Medical Inc., an Edmonton-area company that develops medical devices based on nitric oxide technology.

"I found out about PulmoNOx from a friend who has a job there," he says. "His work sounded really interesting. My university studies [Ghaffari has a B.Sc. in biochemistry] focused mainly on sciences, but I never–or rarely–heard about the end points of research. I wanted to learn more about the whole area of commercializing technology.

"There is a lot of great research done in Canada, but our biotechnology sector is very young. We need more people who understand the business side and can move products along to commercialization."

The internship program supports training in technology commercialization and is available to individuals with an appropriate background in science or business–or both. AHFMR funds the salary of the intern and provides a training allowance. The host company is expected to give the intern hands-on experience.

That's exactly what Ghaffari is getting at PulmoNOx. Since starting as an intern in October 2000, he has been exposed to product development, marketing, intellectual property protection, and regulatory affairs. Ghaffari hopes to do a second year of internship. "My first year was like basic training in technology commercialization," he says. "I see the second year as pay-back time, when I'll apply what I've learned."

Unlike Ghaffari, TC Intern Lori Querengesser was able to dive directly into commercialization. Because she has an M.B.A. (with a specialization in technology commercialization) in addition to a B.Sc. degree in medical laboratory science, her internship has focused on "putting what I've learned into practice," Querengesser says. She is Business Development Manager at CHENOMX Inc., a small start-up company with proprietary

"I've written our business plan, developed marketing plans, presented at conferences, and dealt with patents and intellectual property protection. There are very few places where I would get the opportunity to do all this. The internship is a fantastic experience for me."

– TC Intern Lori Querengesser

doing

technology that couples nuclear magnetic resonance (NMR) spectroscopy with analytical software to provide one-step analysis of biological fluids.

"I've written our business plan, developed marketing plans, presented at conferences, and dealt with patents and intellectual property protection," she says. "There are very few places where I would get the opportunity to do all this. The internship is a fantastic experience for me."

This sentiment is echoed by Jennifer Lukomskyj, who began working as a TC intern at Micralyne Inc. two years ago. The company specializes in the design and fabrication of micromachined glass, silicon, and thin film components. Lukomskyj, who has a B.Sc. degree and a college business diploma, was hired as Product Manager for Micralyne's Biosystems Division when her internship was completed.

"When I began my job search in 1999, I identified Micralyne as one of my ideal employers, where I could apply my training in both biology and business," she says. "I applied for a position, but my lack of experience prevented me from securing the job. Fortunately, AHFMR offered to provide TC internship funding.

"Employers take a risk when they hire someone just out of school like I was. The TC program helps minimize the risk. It gave me a foot in the door, so I could show Micralyne what I was capable of."

Dr. Marita Hobman also refers to the TC program as a "foot in the door." With a Ph.D., an M.B.A., and years of experience as a research scientist, you wouldn't think Hobman needed any help opening doors. "But my goal was to work on the business side of science, rather than in research," she says. "I was over-educated and under-experienced for this line of work. The TC internship was instrumental in giving me the credibility and experience I needed to get my current job."

Hobman works as Director of Intellectual Property Management at Biomira Inc., a developer of cancer vaccines and one of Alberta's foremost biotechnology companies. For her internship, Hobman worked at the University of Alberta's Industry Liaison Office. She was going to apply for a second year of the TC program, when the Biomira job was offered to her in August 1999. She now has an intern, Dr. Jeff Heibein, working with her.

"Jeff is one of many ambitious, bright individuals with Ph.D.s who don't necessarily want to have an academic career," Hobman notes. "However, they need to have experience working on the business side. How are they going to get it? The TC program fills a gap in training.

"If we're going to build the biotechnology industry in Canada, we'll need more people who have a solid scientific background and business experience in biotechnology. This combination is hard to find, so we must take the initiative and develop these people. The TC program makes a difference."

"If we're going to build the biotechnology industry in Canada, we'll need more people who have a solid scientific background and business experience in biotechnology."
— former TC intern Dr. Marita Hobman

ONE DRINK *is too many*

BABIES HARMED PRIOR TO BIRTH BY THEIR PREGNANT MOTHERS DRINKING ALCOHOL START LIFE SLOWER THAN HEALTHY INFANTS DO – AND THEY NEVER CATCH UP.

"It all happens within the womb," says medical researcher Dr. Robert Sutherland. "We're talking about something that could happen within the first couple of months of pre-natal life of a person that will change how their brain works forever." Fetal Alcohol Syndrome (FAS) is a well-recognized severe condition that results when a pregnant woman consumes high amounts of alcohol in early pregnancy. FAS includes profound psychological and behavioural impairments in infants, and a characteristic "FAS face." Babies are born with a small skull, small and low-set eyes, no bridge to the nose and very thin lips.

FAS is relatively rare, occurring in perhaps one in every 100,000 births, says Dr. Sutherland, professor of psychology and neuroscience at the University of Lethbridge

Less obvious than FAS–but likely 10 times more common–are mental and physical impairments caused by exposure in the womb to much lower doses of alcohol than those associated with FAS, he says. Medical scientists now categorize this more subtle, but permanent, damage as alcohol-related neuro-developmental defects.

DR. ROBERT SUTHERLAND

Even with the best cognitive rehabilitation programs, which Dr. Sutherland says are beneficial, "it's very important to realize that these deficits are lifelong." They affect hundreds of thousands of people, and represent the "biggest preventable cause of retardation and cognitive impairment in Canada."

Dr. Sutherland is investigating the biological systems in the fetal brain which involve memory and learning, and that are permanently blunted by relatively low daily doses of alcohol. He and his colleagues work with an animal model– the laboratory rat. Mother rats are fed a nutritious liquid, containing alcohol, throughout pregnancy. The alcohol concentration and dose are much lower than the levels associated with FAS, to simulate an alcohol-addicted pregnant woman's nightly pattern of drinking.

The mother rat "is drinking a lower alcohol concentration than beer," Dr. Sutherland says. As soon as the rat pups are born, they're separated from their drinking mother and raised in a normal environment by healthy mothers that have never drank alcohol. By using this "cross-fostering approach," pioneered by research collaborator Dr. Dan Savage at the University of New Mexico, "we can say exactly what's due to rearing and exactly what's due to the actual drug in the brain during development," Dr. Sutherland explains.

His research includes measuring the neurochemical changes that occur in the rats' brains as the animals develop. Alcohol-exposed animals show lifelong deficits in "synaptic plasticity response" or in how their brains retain and adapt to experiences. Neurotransmitters or brain messenger chemicals that regulate this response are disrupted.

Dr. Sutherland also tests the alcohol-exposed rats' memory and learning ability. The animal is placed in a small, walled, circular swimming pool that contains an elevated island hidden just below the surface of opaque-coloured water. Rats that haven't been pre-natally exposed to alcohol quickly learn to swim directly to the island even when it is relocated in the pool. Rats that have been exposed in the womb to alcohol, however, need many tries before they finally catch on to this "memory game."

His research has found that a key chemical receptor, called GABAa, appears to be permanently

disabled in the brain circuitry of alcohol-affected rats. The receptor plays a crucial role in helping the brain adjust to learning situations. The result is that the animals "are not able to adjust as a result of new information," Dr. Sutherland says. Significantly, the same thing is seen in people who suffer memory and learning problems after being pre-natally exposed to alcohol, he notes.

Dr. Sutherland and colleagues at the University of Lethbridge's new Canadian Centre for Behavioural Neuroscience are now expanding their work with the animal model into studies with people. The centre has acquired a dense-array electroencephalograph machine, similar to a standard EEG machine that records the electrical activity in a person's brain. The dense-array unit has many more highly sensitive sensors that are geometrically arranged on the scalp. Study participants, as they sit in front of a computer screen and see faces of familiar people or strangers, generate recognizable brain wave patterns from specific locations in the brain.

These patterns, when coupled with a standard MRI image of the brain, enable researchers to produce a three-dimensional map of each individual's brain as memory and learning are being tested. "Just like a road map of Alberta," Dr. Sutherland says. "So you end up looking and saying this region right here is the place where you see a memory effect."

Researchers, using their animal model data, can then compare the alcohol-affected regions in the brains of rats with those locations in the brains of people who have been similarly exposed and who show memory and learning problems. Sutherland says the goal is to develop methods that will allow physicians to diagnose the impaired mental functioning in people whose brains were affected by alcohol, yet who show no obvious signs of FAS. Within a few years, he expects the research also will help in designing and testing drugs to treat specific damaged regions or systems in people's brains.

Dr. Sutherland and his colleagues have found lifelong memory and learning deficits in rat pups, even when their drinking pregnant mother's blood-alcohol levels remain well below the equivalent legal limit for impairment in people. Although he says it's difficult to generalize this finding to humans, "what it implies is that there's no safe level of alcohol that a woman can drink" while pregnant.

Dr. Sutherland did his post-doctoral work with University of Lethbridge medical researchers Dr. Bryan Kolb and Dr. Ian Whishaw, both internationally recognized as leaders in behavioural neuroscience. "They were instrumental in actually focusing some of the behavioural neuroscience work I was doing to human neuropsychology issues," Dr. Sutherland says.

After spending 10 years at the University of New Mexico, Dr. Sutherland returned this summer to Alberta. He says a big draw was the U of Lethbridge's new $8-million behavioural neuroscience centre. The Alberta Heritage Foundation for Medical Research contributed about $1.4 million toward establishing the centre.

"It is an incredible facility, a large designated space for up to 10 behavioural neuroscience programs," says Dennis Fitzpatrick, U of L's Associate Vice-President of Research. "If we didn't build this building, we would not have been able to attract Rob Sutherland back."

Dr. Sutherland is a Heritage Medical Scientist and also receives funding from the National Institutes of Health and the U.S.-based National Foundation for Functional Brain Imaging.

Recent publications:

Sutherland RJ, McDonald RJ, Savage DD. Prenatal exposure to moderate levels of ethanol can have long-lasting effects on learning and memory in adult offspring. *Psychobiology*. Vol. 28 (4): 532-539. 2000.

Sutherland RJ, McDonald RJ, Savage DD. Prenatal exposure to moderate levels of ethanol can have long-lasting effects on hippocampal synaptic plasticity in adult offspring. *Hippocampus*. Vol. 7: 232-238. 1997.

Improving gait

Walking. Most of us do it every day without giving it a second thought. AHFMR Student Carol Scovil spends most of her time not only thinking about people walking, but also watching and analyzing how people walk.

Carol uses computer simulation to study normal and pathological walking patterns. Her tools include a high-speed "movement capture" system (the same technology used by the film animation industry), and a computer model originally created in the University of Calgary's Human Performance Lab to test running shoes and model ankle sprains. Her studies involve taping reflective markers on human subjects—three each on the foot, lower leg, upper leg, and pelvis—and having them walk across a force plate. Digital video cameras measure the subjects' movements, and the plate records the forces and pressure. "We can reconstruct how they move and some of the forces involved, and we can compare both movement patterns and forces between normal walkers and abnormal walkers," she says.

After completing her B.Sc. in Engineering Physics at Queen's University, Carol came to the University of Calgary, attracted by the excellent reputation of its Biomechanics department. She began as a master's student in the lab of Dr. Janet Ronsky, an Associate Professor of Mechanical and Manufacturing Engineering who studies the knee joint and

Ultimately Carol and her colleagues would like to see their work used as a diagnostic tool more often by surgeons.

does clinical gait research. Looking for an area of study that combined the best of both these areas, Carol became interested in studying the motion of walking. After a year and a half, she switched into a doctoral program to continue her work and is now pursuing a Ph.D. in Mechanical Engineering with a specialty in Biomechanics.

Carol performs her clinical gait studies in the Joint Injury and Arthritis Research Group lab at the McCaig Centre. There she examines the gaits of people with various traumatic injuries and conditions that have been shown to lead to arthritis. Most recently, Carol has been studying subjects with rotational malunion in the tibia, which can occur when a broken leg is set with a nail and the bottom half of the leg rotates in relation to the top half. "For a while we were getting all the patients who have had this nailing procedure in their leg," says Carol. "We were trying to see if there was a link between the amount of malrotation and damaging levels of force in the joint." Carol has also been involved in studies of subjects with scoliosis and worked at evaluating braces for unstable knees.

Surgeons have already used this type of gait analysis in determining surgical procedures on cerebral palsy patients, and ultimately, Carol and her colleagues who work on gait analysis would like to see surgeons use their work as a diagnostic tool more often. However, Carol says, most of the work on gait analysis is still being pursued at a very basic research level.

As for what Carol's future holds, she is still undecided. Continuing in academia is a possibility, as is working for a medical devices company or perhaps a sports equipment company.

In addition to her AHFMR studentship, Carol Scovil holds an NSERC PGS-B scholarship, as well as a Silver Anniversary Graduate Fellowship and a Graduate Studies Fee Scholarship from the University of Calgary. She is also the recipient of the Claudette MacKay-Lassonde Scholarship awarded by the Canadian Engineering Memorial Foundation to commemorate the Montreal massacre.

Recent publication:

Scovil CY, Ronsky JL, Cole GK. Evaluation of a single leg forward dynamics simulation of walking using pelvis drivers. *Proceedings of the VIII International Symposium on Computer Simulation in Biomechanics*, July 4-6, 2001; Milan, Italy.

ABOVE AND LEFT: CAROL SCOVIL

reader resources

Prevention and early intervention: new approaches in mental health

The Early Psychosis Treatment and Prevention Program of the Calgary Health Region:
http://www.ucalgary.ca/cdss/epp

Prevention through Risk Management and Education (PRIME):
Phone: (403) 670-4836

For information on depression:
http://www.depression.org.uk/main/about/aboutindex.html

http://www.info.hc-sc.gc.ca

http://www.cpa.ca/factsheets/main.htm

http://www2.camh.net/CLARKEPages/about_illnesses/depression_facts.html

For information on eating disorders:
Eating Disorder Education Organization
http://www.edeo.org
http://www.nedic.on.ca
http://www.edap.org

Aiming at cancer

Cancer Biology Research Group:
http://www.cancer.ucalgary.ca

Improving gait

Joint Injuries and Arthritis Research Group (JIARG):
http://joint.mccaig.ucalgary.ca/jiarg

Learning by doing

AHFMR Technology Commercialization Internship Program:
http://www.ahfmr.ab.ca/tc/tc-internship.shtml
Phone: (780) 423-5727

Finding ways to help the most challenging patients

U of A Faculty of Medicine and Dentistry, Department of Psychiatry Research:
http://www.med.ualberta.ca/psychiatry/research

The body's pipelines

Lymphovenous Canada:
http://www.lymphovenous-canada.ca

One drink is too many

Alcohol Related Birth Injury Resource Site:
http://www.arbi.org

Debunking heart health myths

APPROACH Web site:
http://www.approach.org

AHFMR Media Fellows for 2001

Salah Sultan

Engineering student, University of Calgary

I think the best word to describe working at CBC Radio would be "exciting". I interviewed celebrities like the real Dr. Patch Adams, covered news conferences on U of C's latest cancer research breakthroughs, and reported on cutting-edge medical technologies. In between all of that, I went to the streets to ask Calgarians what they thought about issues as diverse as a proposed fat tax and back-to-school fashions.

My final big story was on a virtual-reality visor which helps normal folks understand what it must be like to have schizophrenia. The video shows a routine day at the pharmacy. But imaginary sounds and images make for a surreal experience. This piece was important for me as I got to try a "voicer" (my voice guiding the piece).

The helpful and friendly workmates made CBC radio a place I'd love to work at again.

Shelby Haque

Medical student, University of Alberta

"Fake it till you make it." These encouraging words came from my wife as I prepared for my first day at the Edmonton Journal. Even though I could tell you about endochondral ossification and myocardial infarction, I didn't know the first thing about journalism. Regardless of my lack of journalistic knowledge, the stethoscope went into storage as I pretended to be Clark Kent for the next 12 weeks.

I soon found out that my view of the profession was highly romanticized. Journalists usually rely on tips and press releases to find newsworthy events. For scientists, working with the media is an excellent opportunity to inform the public about new research.

Lay people may not care about reovirus, but they care about cancer. They may not care about immunosuppressive drugs, but they care about organ transplants.

The most important thing is to understand what news actually is. News is new and exciting, and appeals to the everyday reader. Lay people may not care about reovirus, but they care about cancer. They may not care about immunosuppressive drugs, but they care about organ transplants. We need to translate our research into something the average reader can understand.

As one editor said to me: "Imagine telling your mom the story. Why would she care? What would she want to know?"

Canadian Publications Agreement #1602004

Physicians: please place in your patient waiting rooms.

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